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Association between synthetic sealants and increased complication rates in posterior fossa decompression with duraplasty for Chiari malformations regardless of graft type

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OBJECTIVE Dural sealants are commonly used in posterior fossa decompression with duraplasty (PFDD) for Chiari malformation type I (CMI). Prior evidence suggests that combining certain sealants with some graft material is associated with an increased rate of complications. In 2018, the authors noted an increased rate of symptomatic pseudomeningocele and aseptic meningitis after PFDD in CMI patients. The authors utilized retrospective and prospective analyses to test the hypothesis that complication rates increase with the use or combination of certain sealants and grafts.

METHODS The analysis was split into 2 periods. The authors retrospectively reviewed patients who underwent PFDD for CMI at their center between August 12, 2011, and December 31, 2018. The authors then eliminated use of DuraSeal on the basis of the retrospective analysis and prospectively examined complication rates from January 1, 2019, to August 4, 2021. The authors defined a complication as symptomatic pseudomeningocele, bacterial or aseptic meningitis, cerebrospinal fluid leak, subdural hygroma, hydrocephalus, surgical site infection, or wound dehiscence.

RESULTS From 2011 to 2018, complications occurred in 24.5% of 110 patients. Sealant choice was correlated with complication rates: no sealant (0%), Tisseel (6%), and DuraSeal (15.3%) ($p < 0.001$). No difference in complication rate was noted on the basis of choice of graft material ($p = 0.844$). After eliminating DuraSeal, the authors followed 40 patients who underwent PFDD after 2018. The complication rate decreased to 12.5%. All complications after 2018 were associated with Tisseel.

CONCLUSIONS At the authors' single center, use of sealants in PFDD surgery for CMI, especially DuraSeal, was correlated with a higher complication rate. Eliminating DuraSeal led to a significant decrease in the rate of symptomatic pseudomeningocele and aseptic meningitis.

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KEYWORDS Chiari malformation; dural sealant; duraplasty; DuraSeal; graft

Chiari malformation type I (CMI) occurs in approximately 1% of the pediatric population.[1] Surgery includes 2 main approaches: bone-only posterior fossa decompression or posterior fossa decompression with duraplasty (PFDD). Although PFDD is associated with a higher rate of clinical improvement than bone-only decompression,[2–4] it also carries a higher rate of complications.[2–6] In PFDD, complications occur in approximately 12%–16% of patients[3,7] and can include pseudomeningocele, bacterial or aseptic meningitis, cerebrospinal fluid (CSF) leak, and surgical site infection (SSI). These complications can lead to a longer hospital length of stay and a substantial increase in healthcare-related costs.[8,9]

To decrease the incidence of complications, neurosurgeons have focused on decreasing the rate of CSF leaks by using various types of dural grafts sutured to the native dura mater and occasional augmentation of the closure edges with dural sealants. Surgeons use a variety of graft materials, including autologous[10,11] and nonautologous grafts[12] that can be synthetic,[13,14] as well as collagen-based,[15,16] al-

ABBREVIATIONS BCa = bias-corrected and accelerated; CMI = Chiari malformation type I; CSF = cerebrospinal fluid; IP = intervention period; PFDD = posterior fossa decompression with duraplasty; RP = reference period; SSI = surgical site infection; S1 = surgeon 1.

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lograft,[12,16] and xenograft materials.[17] In an effort to obtain a watertight seal, many surgeons supplement duraplasty with a dural sealant. Several forms of dural sealants are commercially available, including biological, semisynthetic, and synthetic glues, with studies showing mixed results on their efficacy in reducing complications.[18–23]

At our institution, graft and sealant use has varied among neurosurgeons over the years. Prior to 2018, our neurosurgeons used 2 common nonautologous grafts: AlloDerm (BioHorizons, Inc.), an acellular human dural allograft, and Durepair Dura Regeneration Matrix (TEI Biosciences, Medtronic Neurosurgery), a collagen-based graft derived from fetal bovine dermis. Some neurosurgeons augmented duraplasty with 1 of 2 commonly used sealants: Tisseel (Baxter Healthcare Corp.), a human fibrin sealant, and DuraSeal (Integra LifeSciences), a synthetic polyethylene glycol hydrogel dural sealant. The other neurosurgeons did not use sealants.

In 2018, we noted an increase in our postoperative complication rates in patients who underwent PFDD for CMI. Specifically, we noted an increased rate of symptomatic pseudomeningocele and aseptic meningitis. Recognition of an increased complication rate led to a review of our institutional data to identify contributing factors. We hypothesized that the use of certain dural sealants, grafts, or combinations thereof may have contributed to this increased complication rate. Here, we report the results of our retrospective review of data that led to the change in our surgical practice. We also report the results of the prospective review performed after implementation of the intervention from 2019 to 2021.

Recent systematic reviews and meta-analyses have reported on the complication rates of different grafts,[7,24] but only a small number of studies have looked at the effects of sealants and their combination with various grafts on complication rates for PFDD in patients with CMI.[15,22,25,26] Furthermore, this is the first study on the subject to describe a change in practice based on the results of a retrospective study and to confirm that the change in practice led to improvement in complication rates.

Methods

Patient Population

This study included retrospective and prospective reviews of patient electronic medical records. The study population included all patients with a primary diagnosis of CMI who underwent PFDD between August 12, 2011, and August 4, 2021, at Nationwide Children's Hospital, Columbus, Ohio. Patients who underwent PFDD after failed bone-only decompression were included. Patients with bone-only decompression, prior duraplasty procedure, CMII, skull base anomalies, congenital syndromes causing foramen magnum stenosis, fourth ventricle stents, and central nervous system tumors were excluded (Fig. 1).

Retrospective and Prospective Groups

The reference period (RP) included retrospectively collected data of patients who underwent surgery from August 12, 2011, to December 31, 2018. Review of our CMI patients who underwent PFDD during that time identified

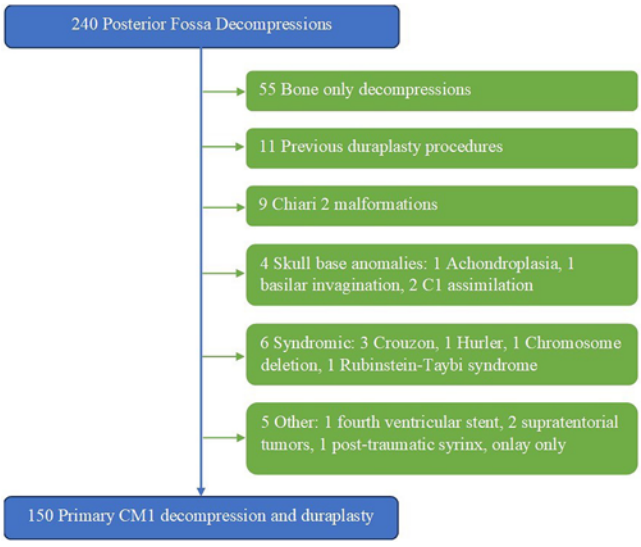

FIG. 1. Patient selection for posterior fossa decompression surgery for CMI from August 12, 2011, to August 4, 2021. Figure is available in color online only.

a potential association between complication occurrence and DuraSeal, especially when combined with Durepair. In January 2019, our neurosurgery department reached a consensus and eliminated the use of DuraSeal during PFDD for CMI, while surgeons continued using either Tisseel or no sealant. The intervention period (IP) included data collected prospectively from January 1, 2019, to August 4, 2021, after we eliminated the use of DuraSeal. The institutional review board at Nationwide Children's Hospital approved both the retrospective and prospective components of the study.

Surgical Technique

The PFDD surgical procedures were performed by 9 neurosurgeons who practiced at Nationwide Children's Hospital between 2011 and 2021. The surgical techniques used for PFDD were similar across all surgeons. The operation was performed with the patient in the prone position and included an occipital craniectomy sized proportionally to the patient's anatomy in order to achieve decompression of the foramen magnum along with C1 laminectomy. The dura was opened in a Y-shaped fashion, and any adhesions or arachnoid bands were released to achieve unobstructed CSF flow from the fourth ventricular outlet to the obex. Tonsillar cauterization was reported for each surgery and included in the analysis.

Each surgeon's individual practice was consistent across cases and did not vary on the basis of intraoperative observation. However, there were practice differences between surgeons with respect to graft and sealant use. The dural substitutes and sealants used during the study period included AlloDerm or Durepair, and Tisseel or DuraSeal, respectively. None of the surgeons used periosteum or fascia as a graft substitute. For all surgeons, the choice of dural substitute or sealant, if any, was based on the surgeon's preference and usual practice pattern prior to January 1, 2019. During this period, 4 surgeons used AlloDerm, 3

TABLE 1. Characteristics, surgical variables, and complications of patients who underwent PFDD for CMI during RP and IP, as well as for the entire cohort

Characteristic	Entire Cohort	RP	IP
Patients	150 (100)	110 (73.3)	40 (26.7)
Age, yrs	10.57 ± 4.71	10.46 ± 4.64	10.88 ± 4.96
Male sex	67 (44.7)	49 (44.5)	18 (45)
Indication for surgery*			
Only CMI	66 (44)	50 (45.4)	16 (40)
Plus scoliosis	29 (19.3)	22 (20)	7 (17.9)
Plus syrinx	73 (48.7)	53 (48.2)	20 (51.3)
Plus other condition	5 (3.3)	1 (0.9)	4 (10.3)
Prior bone-only decompression	13 (8.7)	11 (10)	2 (5)
Tonsillar cauterization	112 (74.7)	77 (70)	35 (87.5)
Graft			
AlloDerm	78 (52)	52 (47.3)	26 (65)
Durepair	72 (47)	58 (52.7)	14 (35)
Sealant			
No sealant	31 (20.7)	9 (8.2)	22 (55)
Tisseel	45 (30)	27 (24.5)	18 (45)
DuraSeal	74 (49.3)	74 (67.3)	0
Onlay			
None	104 (69.3)	92 (83.6)	12 (30)
Muscle	16 (10.7)	12 (10.9)	4 (10)
Gelfoam	3 (2)	3 (2.7)	0
DuraGen	21 (14)	3 (2.7)	18 (45)
Muscle & DuraGen	6 (4)	0	6 (15)

Values are shown as number (%) or mean ± SD unless indicated otherwise.
* The total number (%) exceeds 150 (100%) because some patients had more than 1 indication for surgery in addition to CMI (e.g., presence of scoliosis and syrinx in the same patient).

used Durepair, and 1 used either AlloDerm or Durepair. Two surgeons did not use a sealant, 3 used DuraSeal, 1 used Tisseel, and 1 used either Tisseel or DuraSeal. After January 1, 2019, all surgeons stopped using DuraSeal as a sealant but continued to use Tisseel or no sealant and Durepair or AlloDerm as a graft on the basis of their usual practice patterns. On January 1, 2020, all our surgeons also stopped using Durepair as a graft because of the publication of the Park-Reeves Syringomyelia Research Consortium study data.[24] Any additional onlay grafting material, which included autologous muscle to re-enforce any site of CSF leak after duraplasty, Gelfoam (Pfizer), and DuraGen matrix (Integra LifeSciences Corp.), was also recorded and included in the analysis.

Complications

Recognized complications occurred within 90 days after surgery and included development of symptomatic pseudomeningocele, aseptic meningitis, bacterial meningitis, CSF leak, hydrocephalus, SSI (i.e., incision changes that required a course of antibiotics or operative intervention), and wound dehiscence. If more than 1 complication occurred in the same patient, this was considered a single complication event and the rate of each complication was separately reported. Pseudomeningocele was considered symptomatic if it was associated with CSF leak, prompted the patient to seek medical attention due to pain, or required readmission for further management; those cases noted during routine clinic follow-up without associated symptoms were considered asymptomatic and not included in the current study.

Statistical Analysis

Statistical analysis was completed using IBM SPSS Statistics version 28 (IBM Corp.). Categorical variables were assessed for independence with the Pearson's chi-square test or Fisher's exact test where appropriate, and effect size was estimated with Cramér's V. The complication rates of the surgical variables for the whole cohort were analyzed to reduce the chance of a type II error, and results were confirmed between the retrospective and prospective groups by using bias-corrected and accelerated (BCa) bootstrap 95% CIs with 1000 samples when possible. Onlay use was grouped into "no onlay" and "onlay" due to the small numbers in the latter group for ease of analysis.

Univariant analysis and multivariant logistic regression analysis of the surgical variables and complications were performed. The 2 most common complications, symptomatic pseudomeningocele and aseptic meningitis, were also included in the analysis. More than 1 model was used because surgeon 1 (S1) performed the largest proportion of surgical procedures (35.5%) and used DuraSeal during the RP (72.5% of cases with DuraSeal use); therefore, these 2 variables were very strongly correlated (Cramér's V = 0.778) and entered separately in the multivariant analysis. This surgeon used no sealant during the 1st year of IP and used Tisseel thereafter. A third model was used to assess the combination of sealant and graft on complication rates. The Nagelkerke R^2 value is reported for each model. All statistical tests were 2-tailed, with $p < 0.05$ considered significant.

Results

Cohort Characteristics

A total of 150 patients met the inclusion criteria (Fig. 1). The mean (range) age was 10.6 (1–19) years, and 44.7% of patients were male. Patient characteristics and surgical variables are presented in Table 1. Complications occurred in 21.3% of patients over the entire study period (Table 2), and the 2 most frequent complications were symptomatic pseudomeningocele (12.7%) and aseptic meningitis (9.3%). The rate of CSF leakage was 2.7%. Complications occurred at a mean ± SD (range) 23 ± 12.67 (5–49) days postoperatively.

The majority of patients with pseudomeningocele were managed conservatively, 2 required revision at the operative site (1 of which was associated with a CSF leak), and 2 required transient CSF diversion (both associated with CSF leak). Three patients had shunted hydrocephalus prior to decompression, which was investigated for patency before considering posterior decompression. The 5 postoperative hydrocephalus cases included 1 postoperative shunt

TABLE 2. Complication rates of the entire cohort, and comparison between RP and IP

Complication	All (n = 150)	RP (n =110)	IP (n = 40)	p Value	OR (BCa 95% CI)
Any complication	32 (21.3)	27 (24.5)	5 (12.5)	0.122	0.439 (0.095–1.089
Symptomatic pseudomeningocele	19 (12.7)	18 (16.4)	1 (2.5)	**0.025**	0.131 (0.084–0.604)
Aseptic meningitis	14 (9.3)	14 (12.7)	0	**0.022**	
Bacterial meningitis	1 (0.7)	1 (0.9)	0	>0.99	
CSF leak	4 (2.7)	3 (2.7)	1 (2.5)	>0.99	0.915 (0.415–6.197)
Hydrocephalus	5 (3.3)	3 (2.7)	2 (5)	0.61	1.877 (0.47–10.717)
SSI	7 (4.7)	5 (4.5)	2 (5)	>0.99	1.105 (0.299–6.125)
Wound dehiscence	2 (1.3)	1 (0.9)	1 (2.5)	0.464	2.795 (0.725–10.688)

Values are shown as number (%) unless indicated otherwise. Boldface type indicates statistical significance ($p < 0.05$).

malfunction that required revision, 2 endoscopic third ventriculostomy procedures, 1 placement of a temporary external ventricular drain, and 1 case of transient ventriculomegaly that was successfully managed conservatively.

Complications Before and After Change in Practice

In the RP, complications occurred in 24.5% of patients, with the highest proportion among those treated with DuraSeal (20.9%), whereas no complications occurred in the no-sealant group ($p = 0.049$). Symptomatic pseudomeningocele and aseptic meningitis also occurred more frequently in the DuraSeal group, but the difference was only significant for symptomatic pseudomeningocele ($p = 0.027$ and 0.112, respectively). Complications occurred less frequently in the IP (12.5%), but this rate was not significantly different from the rate in the RP ($p = 0.122$). However, the rates of symptomatic pseudomeningocele (2.5%, $p = 0.025$) and aseptic meningitis (0%, $p = 0.022$) were significantly lower in the IP (Table 2). Complications during the IP were also higher with Tisseel use compared with no sealant use (12.5 vs 0%, respectively; $p = 0.013$). The complication rate for S1 decreased from 12.7% in RP to 5% in IP. There were no significant differences between the complication rates of either period based on graft type or other surgical variable, including surgeon, prior bone-only decompression, tonsillar cauterization, and onlay use (Table 3).

Analysis of Complications Related to Graft and Sealant USE

AlloDerm was used in 52% and Durepair in 47% of patients. The complication rates were equal between the 2 grafts (10.7%, $p = 0.844$). Duraplasty was supplemented with a sealant in 79.3% of patients (30% were Tisseel patients and 49.3% DuraSeal patients). There were significantly different rates of any complication according to sealant use, as well as rates of symptomatic pseudomeningocele and aseptic meningitis; all complication rates were highest among patients treated with DuraSeal (Table 3). There were no complications in the no-sealant group.

Subgroup analysis of complications among sealants showed higher rates of symptomatic pseudomeningocele (14.3% vs 1.7%, $p = 0.009$, OR 6.412, BCa 95% CI 1.943–18.438) and aseptic meningitis (10.9% vs 0.8%, $p = 0.016$, OR 9.377, BCa 95% CI 1.854–15.543) with DuraSeal use compared with Tisseel. The rate of CSF leaks did not significantly differ with the use of sealant compared with no sealant (2.7% vs 0%, respectively, $p = 0.581$). There were significantly different rates of any complication, symptomatic pseudomeningocele, and aseptic meningitis among the sealant and graft combinations; all complication rates were highest when DuraSeal was combined with any graft (Table 3), but the most notable rate was that of aseptic meningitis among patients who received the combination of DuraSeal and Durepair (Fig. 2).

Multivariant logistic regression was performed to assess the relationships between surgical variables and complication rates. More than 1 model was used to assess the factors associated with the occurrence of any complication, symptomatic pseudomeningocele, and aseptic meningitis (see *Statistical Analysis*). The DuraSeal model explained 9.4% (Nagelkerke R^2) of the variance in complication rates and correctly classified 78.7% of cases. DuraSeal was 3.1 times more likely to be associated with a complication in our multivariant analysis than Tisseel and no sealant. No other surgical variable was associated with a complication in our multivariant analyses (Table 4).

Discussion

To our knowledge, this is the first study to report prospective results after a change in practice in CMI surgery. We found, from our retrospective analysis, that DuraSeal was associated with a significant increase in the rate of overall complications. After eliminating the use of DuraSeal, we noted significant decreases in the rates of symptomatic pseudomeningocele and aseptic meningitis. We did not find a difference in complication rates between the 2 dural grafts. However, the combination of DuraSeal and any graft had a higher rate of overall complications. In particular, the combination of DuraSeal with Durepair was associated with a significantly higher rate of aseptic meningitis. As potential confounding factors, operating surgeon, prior bone-only decompression, tonsillar cauterization, and use of an onlay did not have significant effects on the complication rates in our multivariant logistic regression models.

Effect of Dural Sealants

Our results show that DuraSeal had higher rates of any

TABLE 3. Complication rates and univariant analysis of the surgical variables for the entire cohort, RP, and IP

Characteristic	Any Complication*			Symptomatic Pseudomeningocele*			Aseptic Meningitis*		
	RP	IP	Overall	RP	IP	Overall	RP	IP	Overall
Surgeon†									
1 (n = 51)	14 (12.7)	2 (5)	16 (10.7)	11 (10)	1 (2.5)	12 (8)	9 (8.2)	0	9 (6)
2 (n = 26)	2 (1.8)	2 (5)	4 (2.7)	0	0	0	1 (0.9)	0	1 (0.7)
3 (n = 9)	2 (1.8)	1 (2.5)	3 (2)	0	0	0	1 (0.9)	0	1 (0.7)
4 (n = 15)	2 (1.8)	0	2 (1.3)	1 (0.9)	0	1 (0.7)	1 (0.9)	0	1 (0.7)
5 (n = 6)	NA	0	0	NA	0	0	NA	0	0
6 (n = 29)	7 (6.4)	NA	7 (4.7)	6 (5.5)	NA	6 (4)	2 (1.8)	NA	2 (1.3)
7 (n = 7)	0	NA	0	0	NA	0	0	NA	0
8 (n = 6)	0	NA	0	0	NA	0	0	NA	0
9 (n = 1)	0	NA	0	0	NA	0	0	NA	0
p value‡	0.622	0.269	0.307	0.166	>0.99	0.06	0.435		0.635
Effect size§	0.285	0.271	0.265	0.318	0.245	0.322	0.26		
Prior bone compression									
No. (%)	2 (1.8)	0	2 (1.3)	2 (1.8)	0	2 (1.3)	1 (0.9)	0	1 (0.7)
p value‡	>0.99	>0.99	0.736	>0.99	>0.99	0.671	>0.99		>0.99
Effect size§	0.049	0.087	0.045	0.016	0.037	0.025	0.036		0.017
OR (BCa 95% CI)¶	0.658 (0.193–2.691)		0.648 (0.196–2.174)	1.153 (0.339–4.969)		1.283 (0.373–5.082)	0.662 (0.354–3.834)		0.0795 (0.426–3.98)
Onlay**									
No onlay	23 (20.9)	3 (7.5)	26 (17.3)	17 (15.5)	0	17 (11.3)	11 (10)	0	11 (7.3)
Muscle	4 (3.6)	0	4 (2.7)	1 (0.9)	0	1 (0.7)	3 (2.7)	0	3 (2)
Gelfoam	0	NA	0	0	NA	0	0	NA	0
DuraGen	0	2 (5)	2 (1.3)	0	1 (2.5)	1 (0.7)	0	0	0
Muscle & DuraGen	NA	0	0	NA	0	0	NA	0	0
p value‡	>0.99	0.149	0.131	0.297	>0.99	0.06	0.583		0.552
Effect size§	0.024	0.247	0.135	0.129	0.105	0.166	0.052		0.064
OR (BCa 95% CI)¶	0.857 (0.184–2.611)	0.231 (0.045–1.651)	0.45 (0.119–1)	0.26 (0.15–1.35)		0.233 (0.076–0.786)	1.473 (0.0339–6.179)		0.59 (0.147–1.967)
Tonsillar cauterization									
No. (%)	18 (16.4)	5 (12.5)	23 (15.3)	11 (10)	1 (2.5)	12 (8)	11 (10)	0	11 (7.3)
p value‡	0.809	>0.99	0.655	0.405	>0.99	0.26	0.547		>0.99
Effect size§	0.041	0.143	0.033	0.086	0.061	0.101	0.071		0.029
OR (BCa 95% CI)¶	0.814 (0.29–2.699)		0.833 (0.348–2.446)	0.619 (0.216–1.77)	—	0.531 (0.146–2.452)	1.667 (0.462–7.372)		1.271 (0.352–5.323)
Graft									
All	13 (11.8)	3 (7.5)	16 (10.7)	9 (8.2)	1 (2.5)	10 (6.7)	4 (3.6)	0	4 (2.7)
Dur	14 (12.7)	2 (5)	16 (10.7)	9 (8.2)	0	9 (6)	10 (9.1)	0	10 (6.7)
p value‡	>0.99	>0.99	0.844	0.803	>0.99	>0.99	0.16		0.091
Effect size§	0.01	0.04	0.021	0.024	0.118	0.005	0.143		0.15
OR (BCa 95% CI)¶	0.955 (0.389–2.367)	1.278 (0.285–8.307)	1.107 (0.48–2.681)	0.878 (0.3–2.484)		0.971 (0.282–3.189)	2.5 (0.761–10.991)		2.984 (0.959–13.388)

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TABLE 3. Complication rates and univariant analysis of the surgical variables for the entire cohort, RP, and IP

Characteristic	Any Complication*			Symptomatic Pseudomeningocele*			Aseptic Meningitis*		
	RP	IP	Overall	RP	IP	Overall	RP	IP	Overall
Sealant									
No sealant	0	0	0	0	0	0	0	0	0
T	4 (3.6)	5 (12.2)	9 (6)	1 (0.9)	1 (2.5)	2 (1.3)	1 (0.9)	0	1 (0.7)
Dur	23 (20.9)	NA	23 (15.3)	17 (15.5)	NA	17 (11.3)	13 (11.8)	NA	13 (8.7)
p value‡	**0.049**	**0.013**	**<0.001**	**0.027**	0.45	**<0.001**	0.112		**0.002**
Effect size§	**0.234**	**0.418**	**0.29**	**0.257**	0.177	**0.309**	0.21		**0.281**
Graft & sealant									
All & NS	0	0	0	0	0	0	0	0	0
All & T	1 (0.9)	3 (7.5)	4 (2.7)	1 (0.9)	1 (2.5)	2 (1.3)	0	0	0
All & D	12 (10.9)	NA	12 (8)	8 (7.3)	NA	8 (5.3)	4 (3.6)	NA	4 (2.7)
Dur & NS	0	0	0	0	0	0	0	0	0
Dur & T	3 (2.7)	2 (5)	5 (3.3)	0	0	0	1 (0.9)	0	1 (0.7)
Dur & D	11 (10)	NA	11 (7.3)	9 (8.2)	NA	9 (6)	9 (8.2)	NA	9 (6)
p value‡	0.194	**0.043**	**0.01**	0.06	0.625	**0.004**	0.197		**0.015**
Effect size§	0.238	**0.418**	**0.294**	0.271	0.26	**0.322**	0.263		**0.321**

All = AlloDerm; D = DuraSeal; Dur = Durepair; NA = not applicable; NS = no sealant; T = Tisseel.

Values are shown as number, number (%), or mean ± SD unless indicated otherwise. Boldface type indicates statistical significance ($p < 0.05$).

* Percentages are reported on the basis of the total number of complications.

† The number of PFDD procedures performed by each surgeon is shown.

‡ The p values were calculated for each individual variable for the RP, IP, and overall cohort by using Fisher's exact test.

§ Effect size was calculated with Phi and Cramér's V.

¶ OR (BCa 95% CI) is reported for 2 × 2 tables.

** Onlay was grouped into 2 categories: no onlay and onlay. Values could not be calculated for the empty cells because of the presence of zero values.

complication (15.3%), symptomatic pseudomeningocele (11.3%), and aseptic meningitis (8.7%). A higher complication rate with DuraSeal use was reported by Parker et al., who identified a 50% complication rate in a smaller cohort of 12 of 114 patients; however, this finding was not investigated further with follow-up of complication rates after elimination of DuraSeal use.[25] Menger et al. retrospectively reviewed 150 adult patients who underwent PFDD for CMI with autologous, bovine pericardium, or synthetic dural grafts and found a significant association of pseudomeningocele formation (symptomatic or not) with the use of any sealant (DuraSeal or Tisseel).[26] In a retrospective review of 165 adult patients who underwent PFDD for CMI with an allograft or xenograft, as well as Tisseel or DuraSeal, the authors observed higher rates of pseudomeningocele, CSF leaks, and wound infection in the DuraSeal group at 23.1%, 19.2%, and 15.4%, respectively, but their results did not reach statistical significance.[22] DuraSeal was used in only 26 patients in their cohort, so their study may have been underpowered.

In our study, DuraSeal was used in a greater number of patients, and this increased the power to uncover associations between complications and sealant use. We further showed that sealant use and complications were not related to CSF leak because there were no differences in the CSF leak rates between patients who were treated with a sealant and those who were not treated with one. This implies that future studies on sealant use for dural closure should also analyze the rates of other complications such as pseudomeningocele formation and aseptic meningitis, which are often transient but may lead to significant postoperative treatment costs and healthcare resource utilization. Another consideration for the future treatment of CMI patients may be to abandon sealant use altogether because it does not seem to affect the rate of CSF leaks and may lead to other potential complications.

Effect of Dural Grafts

We did not find a significant difference in the complication rates between Durepair and AlloDerm, despite observing that the rate of aseptic meningitis with Durepair (6.7%) exceeded that with AlloDerm (2.7%). Multiple prior studies have compared outcomes among different grafts with varying results. Bowers et al. compared 4 different nonautologous grafts in 128 patients, which included AlloDerm and Durepair, and found that AlloDerm was associated with lower rates of reoperation due to CSF leak or pseudomeningocele than Durepair, DuraGen, or DuraGuard.[12] They also noted that only 3 cases of aseptic meningitis occurred in patients treated with non-AlloDerm grafts, i.e., DuraGen and DuraGuard. A similar result was shown by Yahanda et al., who used data from the Park-Reeves Syringomyelia Research Consortium in a retrospective review of 781 pediatric patients who underwent PFDD for CMI with syringomyelia.[24] They found a significant difference in the complication rates among the 4 nonautologous grafts included in their analysis, with the second highest rate reported for bovine collagen (34.7%) and the lowest for allograft (14.3%). In contrast to the study by Yahanda et al., we did not find a significant difference in the complication rates between grafts, potentially because our study was underpowered compared with their large-cohort study.[7] On the other hand, these differences were not demonstrated in a recent meta-analysis that included 1461 patients and found no significant differences in the overall complication rates for 5 different graft materials, which included autografts, collagen-based grafts, and allografts.[7] However, the analysis did find a significantly lower rate of pseudomeningocele when comparing autograft to collagen-based grafts and allograft. In addition, the rate of aseptic meningitis was higher among those treated with collagen-based grafts than those treated with autograft; although this difference was not statistically significant.[7]

Complication rates may vary even among different col-

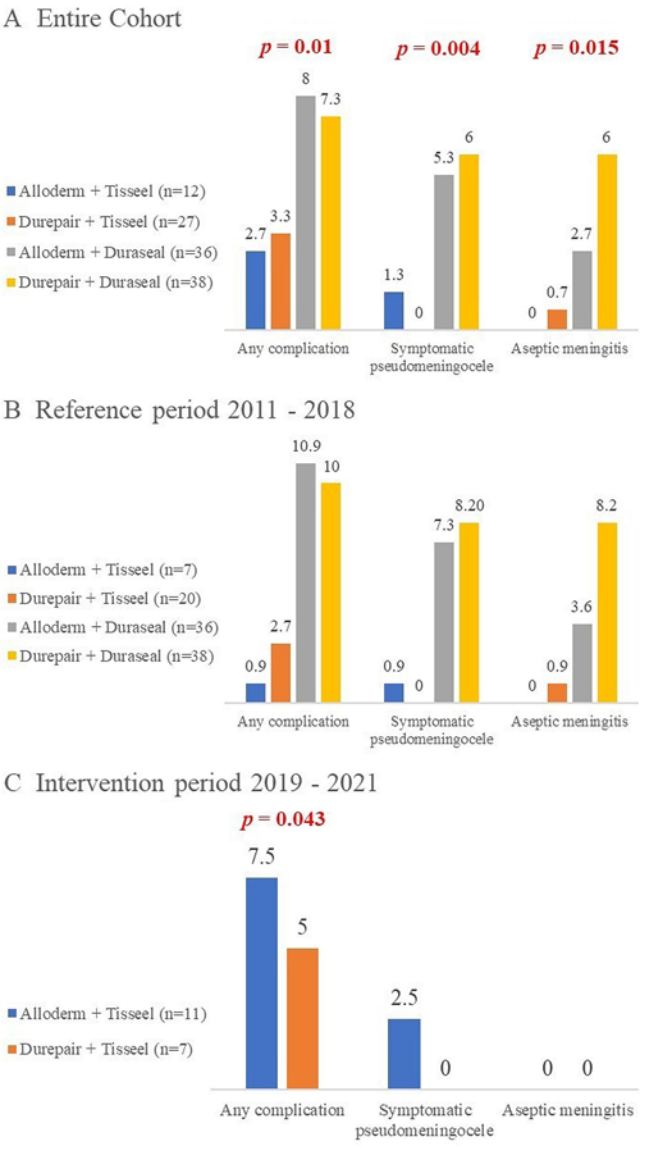

FIG. 2. Complications (percent of total) for the graft and sealant combinations. **A:** Entire cohort. **B:** RP. **C:** IP. The p values were calculated on the basis of the inclusion of the AlloDerm and no-sealant group (24 total patients; 9 in RP and 15 in IP) and Durepair and no-sealant group (7 total patients; 0 in RP and 7 in IP) (not shown), which did not have complications. Figure is available in color online only.

TABLE 4. Multivariant logistic regression of surgical variables related to complications, symptomatic pseudomeningocele, and aseptic meningitis

Variable	Any Complication	Symptomatic Pseudomeningocele	Aseptic Meningitis
Model 1			
Prior bone decompression	0.643; 0.675 (0.128–3.564)	0.856; 1.179 (0.2–6.947)	0.981; 1.028 (0.104–10.193)
No onlay	0.252; 0.519 (0.169–1.594)	0.165; 0.301 (0.055–1.637)	0.808; 0.832 (0.188–3.677)
Tonsillar cauterization	0.47; 0.656 (0.208–2.062)	0.737; 0.802 (0.222–2.9)	0.79; 1.241 (0.252–6.112)
AlloDerm	0.281; 0.568 (0.203–1.588)	0.731; 0.78 (0.19–3.209)	0.278; 2.485 (0.48–12.855)
Surgeon	0.837; NA	0.998; NA	0.908; NA
Nagelkerke R^2	0.119	0.278	0.146
Model 2			
Prior bone decompression	0.524; 0.591 (0.117–2.98)	0.918; 1.094 (0.196–6.104)	0.998; 0.997 (0.1–9.923)
No onlay	0.537; 0.711 (0.424–3.146)	0.547; 0.6 (0.114–3.147)	0.425; 1.901 (0.392–9.214)
Tonsillar cauterization	0.778; 1.155 (0.424–3.146)	0.949; 0.962 (0.294–3.147)	0.629; 1.459 (0.315–6.755)
AlloDerm	0.892; 0.942 (0.396–2.239)	0.791; 0.863 (0.289–2.571)	0.181; 2.483 (0.655–9.415)
DuraSeal	**0.02; 3.096 (1.197–8.005)**	**0.007; 9.215 (1.844–46.06)**	**0.006; 21.244 (2.394–188.519)**
Nagelkerke R^2	0.094	0.193	0.239
Model 3			
Prior bone decompression	0.898; 0.892 (0.154–5.165)	0.845; 1.199 (0.195–7.364)	0.971; 1.136 (0.104–12.391)
No onlay	0.624; 1.369 (0.39–4.797)	0.444; 0.441 (0.054–3.583)	0.131; 4.484 (0.641–31.397)
Tonsillar cauterization	0.335; 0.54 (0.155–1.89)	0.64;0.729 (0.193-2.747)	0.975; 1.026 (0.198–5.322)
Surgeon	0.685; NA	>0.99; NA	0.942; NA
Graft & sealant combination	0.475; NA	>0.99; NA	>0.99; NA
Nagelkerke R^2	0.27	0.33	0.306

Values are shown as p value; OR (95% CI) unless indicated otherwise. Boldface type indicates statistical significance ($p < 0.05$).

lagen-based grafts. Lee et al. found that porcine collagen grafts were associated with the highest rate of complications and pseudomeningocele formation as compared with bovine collagen in their adult CMI series, but no statistically significant difference was detected for CSF leaks or aseptic meningitis.[15] Although our study did not find a difference in the complication rates between the 2 grafts used, our higher rate of aseptic meningitis in the Durepair group and the reported trend of higher complications in the collagen-based graft group made us continue to shift away from using Durepair as a graft material for PFDD.

Effect of Graft and Sealant Combinations

Our results showed significant differences in the rates of overall complications, symptomatic pseudomeningocele, and aseptic meningitis among groups based on graft and sealant combinations; most notably, the rate of aseptic meningitis was highest among patients treated with Durepair and DuraSeal. The outcomes of various combinations of grafts and sealants have been reported in the literature with mixed and conflicting results. Parker et al. retrospectively reviewed 3 different grafts (EnDura, Durepair, and cadaveric pericardium) and 2 sealants (DuraSeal and Tisseel).[25] Their rate of complications was highest when Durepair was combined with DuraSeal; however, this finding did not reach statistical significance due to the small cohort size (the combination was used to treat 9 of 114 patients). In contrast, Lam and Kasper retrospectively reviewed 100 posterior fossa surgical procedures in adults, wherein an autologous graft was used with a dural sealant (DuraSeal or Evicel) and only 1 complication occurred.[27] They reasoned that the complications reported by Parker et al.[25] were likely due to inherent defects in the graft substances, 2 of which were recalled by the Food and Drug Administration (EnDura and Durepair). However, a series of 26 CMI patients who underwent PFDD with cadaveric grafts with fibrin sealant had higher complication rates than those treated with autologous graft without sealant.[28] In this series, all complications occurred in the cadaveric graft and fibrin sealant group, including 9 cases of CSF leak or pseudomeningocele and 2 cases of aseptic meningitis, whereas no complications were reported in the autologous graft with no-sealant group.[28] Balasa et al. reported on 70 adult CMI patients who underwent duraplasty, comparing autologous (pericranium and fascia lata) and nonautologous (DuraGen and Durepair) grafts and 2 methods of fixation (fibrin glue and sutures).[29] They found a 5-fold increase in pseudomeningocele formation when a nonautologous graft was used (52.4%), which was statistically significant; a nonsignificant increase with fibrin glue (43.5%) was noted as compared with sutures (31.9%).[29] The findings of these studies, in addition to ours, suggest that some graft and sealant combinations may have higher rates of complications than others and that the significance of these associations may not be evident in smaller case series.

Some insight into the systemic reactions to these grafts and sealants may have been provided by in vivo animal

studies. A canine study by Zerris et al. found that Durepair had minimal inflammatory reaction with an infiltrate of fibroblasts and macrophages at 1 and 3 months.[30] According to the warnings and precautions on the manufacturer's website, "Animal study results suggest that the foreign body response associated with the use of sealants and hemostatic agents in conjunction with Durepair may be more pronounced than use of Durepair alone."[31] The manufacturer does not specify which types of sealants or hemostatic agents can lead to such a response. We hypothesize that DuraSeal could be a potential culprit. This is supported by the findings of Ito et al., who compared fibrin glue and DuraSeal in rabbits. They showed that granulation tissue and abscess formation were significantly more severe with DuraSeal, with a massive infiltration of neutrophils.[32] These studies, along with our results and others,[25,28] may explain the higher rate of certain complications seen when combining Durepair and DuraSeal.

Study Limitations

This was one of the larger studies to directly assess complication rates and to consider both grafts and sealants. To our knowledge, this represents the first CMI study to include prospective analysis after a change in practice was made and then to report on the subsequent results. It also adds to the limited number of published studies that have considered the use of a sealant in their analysis. The limitations include the retrospective nature of data collection in the RP, as well as unblinded, unrandomized prospective data collection in the IP. Although our analysis included the operating surgeon as a variable, the effect of differences in surgical technique may also play a role in the rate of complications. Additionally, this analysis was limited by its inclusion of only 2 types of grafts and 2 types of sealants. Bias during the IP due to observer effect (i.e., Hawthorne effect) should be considered; however, this alone would not explain the sustained decrease in certain complications after the change in practice.

Conclusions

This study was a result of the increased complication rate seen in our CMI patients treated with PFDD. The results of our study show that sealant use may contribute to postoperative complications in CMI patients treated with PFDD, particularly symptomatic pseudomeningocele and aseptic meningitis. Further appropriately powered studies, including a randomized controlled trial, would better elucidate the effect of sealants and their combination with certain grafts on complication rates in CMI surgery. As new grafts and sealants become commercially available, continuous institutional assessment is necessary to identify any changes in complication rates and adjust practice accordingly.

References

1. Aitken LA, Lindan CE, Sidney S, et al. Chiari type I malformation in a pediatric population. *Pediatr Neurol*. 2009;40(6):449-454.
2. Durham SR, Fjeld-Olenec K. Comparison of posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation Type I in pediatric patients: a meta-analysis. *J Neurosurg Pediatr*. 2008;2(1):42-49.
3. Lu VM, Phan K, Crowley SP, Daniels DJ. The addition of duraplasty to posterior fossa decompression in the surgical treatment of pediatric Chiari malformation Type I: a systematic review and meta-analysis of surgical and performance outcomes. *J Neurosurg Pediatr*. 2017;20(5):439-449.
4. Xu H, Chu L, He R, Ge C, Lei T. Posterior fossa decompression with and without duraplasty for the treatment of Chiari malformation type I-a systematic review and meta-analysis. *Neurosurg Rev*. 2017;40(2):213-221.
5. Lin W, Duan G, Xie J, Shao J, Wang Z, Jiao B. Comparison of results between posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation type I: a systematic review and meta-analysis. *World Neurosurg*. 2018;110:460-474.e5.
6. Chai Z, Xue X, Fan H, et al. Efficacy of posterior fossa decompression with duraplasty for patients with Chiari malformation type I: a systematic review and meta-analysis. *World Neurosurg*. 2018;113:357-365.e1.
7. Yahanda AT, Simon LE, Limbrick DD. Outcomes for various dural graft materials after posterior fossa decompression with duraplasty for Chiari malformation type I: a systematic review and meta-analysis. *J Neurosurg*. 2021;135(5):1356-1369.
8. Grotenhuis JA. Costs of postoperative cerebrospinal fluid leakage: 1-year, retrospective analysis of 412 consecutive nontrauma cases. *Surg Neurol*. 2005;64(6):490-494.
9. Elsamadicy AA, Koo AB, Lee M, et al. Risk factors portending extended length of stay after suboccipital decompression for Adult Chiari I malformation. *World Neurosurg*. 2020;138:e515-e522.
10. Kosnik EJ. Use of ligamentum nuchae graft for dural closure in posterior fossa surgery. Technical note. *J Neurosurg*. 1998;89(1):155-156.
11. Tubbs RS, Wellons JC III, Blount JP, Oakes WJ. Posterior atlantooccipital membrane for duraplasty. Technical note. *J Neurosurg*. 2002;97(2)(suppl):266-268.
12. Bowers CA, Brimley C, Cole C, Gluf W, Schmidt RH. AlloDerm for duraplasty in Chiari malformation: superior outcomes. *Acta Neurochir (Wien)*. 2015;157(3):507-511.
13. Alzate JC, Kothbauer KF, Jallo GI, Epstein FJ. Treatment of Chiari I malformation in patients with and without syringomyelia: a consecutive series of 66 cases. *Neurosurg Focus*. 2001;11(1):E3.
14. Attenello FJ, McGirt MJ, Garcés-Ambrossi GL, Chaichana KL, Carson B, Jallo GI. Suboccipital decompression for Chiari I malformation: outcome comparison of duraplasty with expanded polytetrafluoroethylene dural substitute versus pericranial autograft. *Childs Nerv Syst*. 2009;25(2):183-190.
15. Lee CK, Mokhtari T, Connolly ID, et al. Comparison of porcine and bovine collagen dural substitutes in posterior fossa decompression for Chiari I malformation in adults. *World Neurosurg*. 2017;108:33-40.
16. Danish SF, Samdani A, Hanna A, Storm P, Sutton L. Experience with acellular human dura and bovine collagen matrix for duraplasty after posterior fossa decompression for Chiari malformations. *J Neurosurg*. 2006;104(1)(suppl):16-20.
17. Bejjani GK, Zabramski J; Durasis Study Group. Safety and efficacy of the porcine small intestinal submucosa dural substitute: results of a prospective multicenter study and literature review. *J Neurosurg*. 2007;106(6):1028-1033.
18. Coucke B, Van Gerven L, De Vleeschouwer S, Van Calenbergh F, van Loon J, Theys T. The incidence of postoperative cerebrospinal fluid leakage after elective cranial surgery: a systematic review. *Neurosurg Rev*. 2022;45(3):1827-1845.
19. Esposito F, Angileri FF, Kruse P, et al. Fibrin sealants in dura sealing: a systematic literature review. *PLoS One*. 2016;11(4):e0151533.

20. Kinaci A, Algra A, Heuts S, O'Donnell D, van der Zwan A, van Doormaal T. Effectiveness of dural sealants in prevention of cerebrospinal fluid leakage after craniotomy: a systematic review. *World Neurosurg*. 2018;118:368-376.e1.
21. Kinaci A, Van Doormaal TPC. Dural sealants for the management of cerebrospinal fluid leakage after intradural surgery: current status and future perspectives. *Expert Rev Med Devices*. 2019;16(7):549-553.
22. Galan D, Monuszko K, Sankey EW, et al. Fibrin glue as an adjuvant dural sealant reduces the rate of perioperative complications in posterior fossa decompression with duraplasty: a single center experience in 165 adult Chiari I patients. *J Clin Neurosci*. 2019;68:80-85.
23. Than KD, Baird CJ, Olivi A. Polyethylene glycol hydrogel dural sealant may reduce incisional cerebrospinal fluid leak after posterior fossa surgery. *Neurosurgery*. 2008;63(1)(suppl 1):ONS182-ONS187.
24. Yahanda AT, Adelson PD, Akbari SHA, et al. Dural augmentation approaches and complication rates after posterior fossa decompression for Chiari I malformation and syringomyelia: a Park-Reeves Syringomyelia Research Consortium study. *J Neurosurg Pediatr*. 2021;27(4):459-468.
25. Parker SR, Harris P, Cummings TJ, George T, Fuchs H, Grant G. Complications following decompression of Chiari malformation Type I in children: dural graft or sealant? *J Neurosurg Pediatr*. 2011;8(2):177-183.
26. Menger R, Connor DE Jr, Hefner M, Caldito G, Nanda A. Pseudomeningocele formation following chiari decompression: 19-year retrospective review of predisposing and prognostic factors. *Surg Neurol Int*. 2015;6:70.
27. Lam FC, Kasper E. Augmented autologous pericranium duraplasty in 100 posterior fossa surgeries—a retrospective case series. *Neurosurgery*. 2012;71(2 Suppl Operative):ons302-ons307.
28. Vanaclocha V, Saiz-Sapena N. Duraplasty with freeze-dried cadaveric dura versus occipital pericranium for Chiari type I malformation: comparative study. *Acta Neurochir (Wien)*. 1997;139(2):112-119.
29. Balasa A, Kunert P, Dziedzic T, Bielecki M, Kujawski S, Marchel A. Comparison of dural grafts and methods of graft fixation in Chiari malformation type I decompression surgery. *Sci Rep*. 2021;11(1):14801.
30. Zerris VA, James KS, Roberts JB, Bell E, Heilman CB. Repair of the dura mater with processed collagen devices. *J Biomed Mater Res B Appl Biomater*. 2007;83(2):580-588.
31. Medtronic. Dura Mater Repair. Indications, safety, and warnings. Durepair Dura Regeneration Matrix. Accessed August 3, 2021. https://www.medtronic.com/us-en/healthcare-professionals/therapies-procedures/neurological/dura-mater-repair/indications-safety-warnings.html
32. Ito K, Horiuchi T, Oyanagi K, Nomiyama T, Hongo K. Comparative study of fibrin and chemical synthetic sealant on dural regeneration and brain damage. *J Neurosurg Spine*. 2013;19(6):736-743.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Shaikhouni. Acquisition of data: all authors. Analysis and interpretation of data: Makoshi, Toop, Smith, Shaikhouni. Drafting the article: Shaikhouni, Makoshi, Toop, Smith, Pindrik, Sribnick, Leonard. Critically revising the article: Shaikhouni, Makoshi, Toop, Smith, Shaikhouni. Reviewed submitted version of manuscript: Shaikhouni, Makoshi, Drapeau, Pindrik, Sribnick, Leonard. Approved the final version of the manuscript on behalf of all authors: Shaikhouni. Statistical analysis: Makoshi. Study supervision: Shaikhouni.

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